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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,271	04/12/2001	William Widner	5455.210-US	4969

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EXAMINER
MONSHIPOURI, MARYAM

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,271	WIDNER ET AL.	
	Examiner	Art Unit	
	Maryam Monshipouri	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 74-93 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 78,79,81 and 85 is/are allowed.

6)☒ Claim(s) 74-77,80,82-84 and 86-93 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-73 are canceled. Claims 74-93 are under examination on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 74-77, 80, 82-84,86-88 and 91-93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hung et al. (Mol. Gen. Genet., 219, 129-136, 1989) in view of Lereclus et al. (WO 94/25612, November 1994). Hung teaches a *Bacillus subtilis* cell comprising a DNA construct comprising a consensus bla promoter originated from E.coli, having the sequence TTGACA for the –35 region and TATAAT for the –10 region operably linked to a mouse dihydrofolate reductase (DHFG) encoding gene, prior to this invention. Hung does not teach a DNA construct further comprising an mRNA processing/stabilizing sequence.

Lereclus teaches an expression system operative in Bacillus comprising a CryIIIA gene, under the control of a Bacillus promoter as well as sequences called "downstream region", situated between the promoter and the coding sequence to be expressed and susceptible of acting at the post-transcriptional level during gene expression. Said "Downstream region" can be considered to be an mRNA processing/stabilizing sequence.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to start with the DNA construct of Hung and place the "downstream region" and optionally, CryIIIa gene of Lereclus into said construct in order to successfully express either the mouse DHFG encoding gene or Bacillus thuringiensis CryIIIa gene in all Bacillus cells.

One of ordinary skill in the art is motivated in inserting the "downstream region" of Lereclus into the DNA construct of Hung because such insertion results in mRNA protection thereby to more commercial scale expression of non-endogenous genes in a variety of Bacillus host cells, rendering the invention obvious.

Finally, one of ordinary skill in the art has a reasonable expectation of success in inserting the "downstream region" and optionally, CryIIIa gene of Lereclus into the Bacillus cell and DNA construct of Hung because said downstream region already works successfully in *Bacillus subtilis* (see claim 40).

Claims 89-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Hung et al. (Mol. Gen. Genet., 219, 129-136, 1989, cited above) in view of Lereclus et al. (WO 94/25612, November 1994, cited above) further in view of Jorgensen et al. (WO 93/10249, issued May 1993).

As stated above, Hung in view of Lereclus teaches a Bacillus cell comprising an extrachromosomal DNA construct comprising a consensus promoter having a sequence TTGACA for the "-35" region and TATAAT for the "-10" region operably linked to a single copy of a reductase encoding gene or CryIIIa gene and an mRNA processing/stabilizing sequence located downstream of the consensus promoter and upstream of said reductase encoding or CryIIIa gene. Hung in view of Lereculs does not teach a Bacillus cell wherein said promoter/gene/mRNA stabilizing construct is contained in the chromosome of the Bacillus cell.

Jorgensen in pages 14-15 teach construction and transfer of a Bacillus licheniformis promoter and a DNA construct comprising said promoter and genes encoding enzymes such as alpha-amylase, protease or glycosyl transferase (see claim 10) into the chormosome of a Bacillus host cell (see the list of Bacillus host cells in claim 15).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to start with the Bacillus host cell of Hung in view of Lereclus and use the instructions, genes (such as amylase or protease encoding genes) and methods of Jorgensen in order to incorporate said construct into the chromosome of the Bacillus cell.

One of ordinary skill in the art is motivated in either using the intact DNA construct of Hung in view of Lereclus or using the construct of Hung in view of Lereclus further in view of Jorgensen wherein the reductase encoding gene of Hung is replaced by amylase or protease encoding genes of Jergenson, for chromosomal integration of a Bacillus host, according to Jergenson. This is because integration of said DNA constructs into the chromosome of the host cell results in a more stable and long term transfection of the host, leading to a recombinant Bacillus host which can express the desired gene for many more generations, rendering the recombinantly expressed products more economical.

One of skill in the art has a reasonable expectation of success in integrating either of the above mentioned DNA constructs into the chromosome of Bacillus host cell according to Jergenson because methods of chromosomal integration of genes in Bacillus and E. coli are well established in the prior art, as evidenced by the disclosure of Jorgensen, rendering the invention obvious.

Allowable Subject Matter

Claims 78-79 , 81 and 85 are allowed. This is because the prior art does not teach or suggest preparing any of the following: **(1)** Bacillus cells comprising an amyQ consensus promoter having a sequence TTGACA for the "-35" region and TATAAT for the "-10" region operably linked to a single copy of a reductase encoding gene or CryIIIa gene and an mRNA processing/stabilizing sequence located downstream of the consensus promoter and upstream of said reductase encoding gene/CryIIIa gene or **(2)** Bacillus host cells according to claim 74, comprising an SP82 mRNA processing stabilizing sequences. Hence said claims are both novel and non-obvious. **(3)** Bacillus host cells according to claims 74, containing no selectable marker genes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maryam Monshipouri whose telephone number is (571) 272-0932. The examiner can normally be reached on 7:00 a.m to 4:30 p.m. except for alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnanthapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

M. Monshipouri

Maryam Monshipouri Ph.D.

Primary Examiner

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